

Citation:

Rodriguez C, Calle EE, Fakhrabadi-Shokoochi D, Jacobs EJ, Thun MJ. Body mass index, height and the risk of ovarian cancer mortality in a prospective cohort of postmenopausal women. *Cancer Epidemiol Biomarkers Prev*. 2002 Sep;11 (9): 822-828.

PubMed ID: [12223425](#)

Study Design:

Prospective Cohort Study

Class:

B - [Click here](#) for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To examine the relationship between body mass index (BMI), height and ovarian cancer mortality among postmenopausal women and whether use of postmenopausal estrogens influenced the relationship.

Inclusion Criteria:

Females participants in the CSP-II, a prospective mortality study begun by the American Cancer Society in 1982.

Exclusion Criteria:

- Women with a history of cancer at the time of enrollment, with the exception of non-melanoma skin cancer
- Women who were pre-menopausal
- Women who had unknown menopausal status
- Women with missing values of height and weight
- Women with extreme values for height, weight or BMI (≤ 0.10 th percentile or ≥ 99.90 th percentile)
- Women who had a hysterectomy or previous ovarian surgery
- Males.

Description of Study Protocol:**Recruitment**

- The CPS-II was established in 1982 and participants were identified and enrolled by volunteers with the American Cancer Society

- All participants, which included 1.2 million women and men, completed a confidential, self-administered questionnaire
- After application of exclusion criteria, a total of 300,537 women and 1,511 ovarian cancer deaths were eligible for analysis.

Design

Prospective cohort study design.

Dietary Intake/Dietary Assessment Methodology

The confidential, self-administered questionnaire included questions regarding dietary exposures. Specific questions not reported.

Blinding Used

Not reported.

Intervention

Not applicable.

Statistical Analysis

- Age-standardized death rates and rate ratios were calculated at each level of BMI and height
- Death rates were directly standardized to the age distribution of the female population of the CPS-II cohort
- Cox proportional hazards modeling was used to compute rate ratios and to adjust for potential confounders
- Stratification for exact year of age at enrollment and control for race (white, non-white), duration of oral contraceptive use, number of full-term pregnancies, age at menarche, age at menopause and status and duration of estrogen replacement therapy was performed for all of the Cox models
- BMI and height were included in all of the Cox models
- Education, family history of breast and/or ovarian cancer and smoking were also examined as potential confounders initially
- The Mantel-Haenszel test for trend was used to determine the statistical significance of the relationship between the risk of ovarian cancer deaths and the levels of increased BMI or height
- Multivariate analysis was completed to test whether any of the potential risk factors influenced the association between BMI and height and ovarian cancer.

Data Collection Summary:

Timing of Measurements

- Participants completed a confidential, self-administered questionnaire in 1982
- Vital status of study participants was determined in 1998 (through personal inquiry of volunteers and automated linkage using the National Death Index).

Dependent Variables

Death from ovarian cancer through December of 1998 as reported by families and through the

National Death Index.

Independent Variables

Responses to self-administered questionnaire (that included personal identifiers, demographic characteristics, personal and family history of cancer and other diseases, reproductive history and other behavioral, environmental, occupational and dietary exposures.

Control Variables

- BMI
- Height
- Age at enrollment
- Race
- Duration of oral contraceptive use
- Number of full-term pregnancies
- Age at menarche
- Age at menopause
- Duration of estrogen replacement therapy.

Description of Actual Data Sample:

- *Initial N*: 300,537 women and 1,511 ovarian cancer deaths were available for analysis
- *Attrition (final N)*: Not applicable
- *Age*: Exact ages not reported. The following was reported:
 - Less than 40 years; N=253
 - 40 to 49 years; N=18,888
 - 50 to 59 years; N=76,852
 - 60 to 69 years; N=55,795
 - Older than 69; N=30,858
- *Ethnicity*:
 - White; N=279,232
 - Other; N=19,716
- *Relevant Demographics*:
 - Education:
 - Less than high school; N=48,297
 - High school graduate; N=92,380
 - Some college; N=84,737
 - College graduate or more; N=69,506
 - Family History of ovarian and/or breast cancer:
 - No; N=276,863
 - Yes; N=23,674
 - Age at menarche:
 - Younger than 12; N=45,571
 - Older than 12; N=240,885
 - Age at menopause:
 - Younger than 40; N=7,812
 - 40-49; N=87,975
 - Older than 50; N=134,527
 - Duration of oral contraceptive use:
 - Never; N=231,746

- Less than five; N=26,641
- More than five; N=26,131
- Duration of estrogen replacement therapy:
 - Non-user; N=176,800
 - Current oral less than 10; N=9,648
 - Current oral more than 10; N=3,834
 - Former oral less than 10; N=34,711
 - Former oral more than 10; N=5,134
- Number of full term pregnancies:
 - None; N=35,890
 - One N=31,090
 - Two to three; N=134,042
 - Four to nine; N=66,482
- Exercise:
 - None; N=7,473
 - Slight; N=66,403
 - Moderate N=201,996
 - Heavy; N=17,566
- Cigarette smoking:
 - Never; N=158,768
 - Current; N=60,351
 - Former; N=58,773
- *Anthropometrics:*
 - Height:
 - Less than 152cm; N=7,005
 - 152 to <157cm; N=34,200
 - 157 to <162cm; N=61,576
 - 162 to <167; N=86,928
 - 167 to <172; N=64,250
 - 172 to <177; N=20,493
 - More than 177cm; N=5,079
 - BMI (kg/m²):
 - Less than 25; N=182,646
 - 25 to <30; N=83,889
 - At least 30; N=34,002
- *Location:* The United States.

Summary of Results:

Number of Deaths and Relative Risks (RR) with 95% Confidence Intervals (CI) of Ovarian Cancer According to BMI			
BMI (kg/m ²)	Number of Deaths	Relative Risks (Adjusted for Age at Entry and Race)	Relative Risks (Adjusted for age at entry, race, height, exercise, age at menarche, age at menopause, duration of oral contraceptive use, status and duration of estrogen replacement therapy use and number of full-term pregnancies)

<18.5	32	99 (0.67-1.45)	098 (0.67-1.45)
18.5 to <20.5	138	1	1
20.5 to <22.0	258	1.19 (0.97-1.46)	1.18 (0.96-1.46)
22.0 to <23.5	226	0.96 (0.77-1.18)	0.95 (0.77-1.17)
23.5 to <25.0	199	0.96 (0.77-1.19)	0.95 (0.76-1.18)
25.0 to <26.5	152	1.00 (0.79-1.26)	1.00 (0.79-1.26)
26.5 to <28.0	174	1.33 (1.06-1.66)	1.32 (1.05-1.65)
28.0 to <30.0	141	1.28 (1.01-1.62)	1.28 (1.01-1.63)
30.0 to <35.0	139	1.21 (0.95-1.53)	1.21 (0.95-1.54)
≥ 35.0	52	1.53 (1.11-2.11)	1.54 (1.12-2.14)

P for trend=0.001

Ovarian Cancer Mortality by BMI and Ever Use of Estrogen Replacement Therapy (ERT)

	Never Used ERT	Used Oral ERT
BMI <25kg/m²		
No. of deaths	462	246
RR (95% CI)	1	1
BMI 25 to <30kg/m²		
No. of deaths	273	95
RR (95% CI)	1.20 (1.03-1.39)	0.99 (0.78-1.26)
BMI ≥ 30kg/m²		
No. of deaths	129	25
RR (95% CI)	1.36 (1.12-1.66)	0.93 (0.62-1.41)
	P for trend=0.001	P for trend=0.001

Other Findings

- Height was positively associated with ovarian cancer mortality and ovarian cancer death rates were lowest among the shortest women (<152cm tall; RR 0.72; 95% CI, 0.47-1.10)
- No evidence found that the association of BMI and height with ovarian cancer mortality was significantly modified by potential confounders.

Author Conclusion:

Results suggest that overweight and obesity are associated with increased risk of ovarian cancer mortality among women who never used postmenopausal estrogen therapy.

Reviewer Comments:

- *Original recruitment methods not specified (other than enrolled by American Cancer Society volunteers)*
- *The authors note the following limitations:*
 - *No direct measure of lean body mass or adiposity*
 - *Heights and weights were self-reported and may not have been accurate*
 - *No information on histological type of ovarian cancer.*

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions

1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions

1.	Was the research question clearly stated?	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	N/A
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes

1.3.	Were the target population and setting specified?	Yes
2.	Was the selection of study subjects/patients free from bias?	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	Were study groups comparable?	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	Yes
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	Was method of handling withdrawals described?	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	???
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A

5.	Was blinding used to prevent introduction of bias?	No
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	No
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	No
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were intervening factors described?	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	N/A
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	N/A
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	N/A
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	N/A
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	Were outcomes clearly defined and the measurements valid and reliable?	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	N/A
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes

7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	Was the statistical analysis appropriate for the study design and type of outcome indicators?	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	Yes
8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	Are conclusions supported by results with biases and limitations taken into consideration?	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes
10.	Is bias due to study's funding or sponsorship unlikely?	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes